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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,606	04/11/2005	Michael Vajdy	PP18892.003	9598

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EXAMINER	
SNYDER, STUART	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,606	VAJDY ET AL.	
	Examiner	Art Unit	
	Stuart W. Snyder	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *3, 17-31, 37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-16 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

REMARKS

Status of claims: Applicants originally submitted a set of 31 claims, two claims each used duplicate numbers and examiner renumbered the claims. Pursuant to the election required by examiner, applicants affirmed the election with traverse of Group 1 (claims 1, 2, and 4-16, in part, drawn to a composition comprising and HIV envelope antigen and LTK63); claims 3 and 17-29 were withdrawn and not examined. In an Office Action of 10/6/2005, the examiner issued a non-final rejection for claims 1, 2, 4-16. In applicants' response of 03/09/2006, applicant added claims 32-40. Claims 32-36 depend on claims 1 and 5; claims 37-40 depend on withdrawn claims and were not examined because of lack of antecedent claims. Applicant further responded to the non-final rejection of 10/6/05 on 5/30/06 rebutting the restriction and the previous 102/103 rejections. Therefore, rebuttal to rejection of claims 1, 2, 4-16 was considered and claims 32-36 were examined.

Restriction requirement: Applicant's election with traverse of Group 1, which corresponds to claims 1,2 and 4-16 drawn to compositions comprising HIV envelope antigens and LTK63, in the reply filed on 3/9/2006 is acknowledged. The traversal is on the ground(s) that certain groups--*e.g.*, groups 1, 3, 5, 7, 8 and 11—relate to a single general inventive concept. That is, there is a common "special technical feature", to wit the composition comprising an HIV envelope antigen and LTK63, wherein the HIV envelope antigen is in an amount of about 0.1 μg to about 1000 μg. This is not found

persuasive because: There is prior art teaching a composition comprising an HIV envelope antigen and LTK63 (Vajdy, *et al.*) and there was no limitation in the original claim about the amount of HIV envelope antigen in the composition.

Applicant argued that examination of Groups 1, 3, 5, 7, 9, and 11 together would not place an undue burden upon the Office. The Office disagrees for the following reasons: Because there is not a shared "special technical feature", each subsequence group would need to be searched independently. For example, Group 3 would require a search for DNA encoding HIV envelope combined with protein adjuvant, including LTK63 whereas Group 5 would require a search for HIV envelope antigen combined with DNA encoding the adjuvant. Clearly these searches are conceptually unrelated: In the first instance a DNA vaccine is combined with protein adjuvant whereas in the second instance a protein vaccine is combined with a DNA sequence encoding an adjuvant (an unprecedented and highly suspect combination).

The requirement is still deemed proper and is therefore made FINAL.

Title: The amended title is acceptable.

Rejection of claims 1, 2, 4-6 and 14-16 Under 35 U.S.C. § 102: Withdrawn.

Rejection of Claims 1, 2, 4-10 and 13-16 Under 35 USC § 103: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 4-10 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vajdy, *et al.* in view of Keefer MC, *et al.* Claims 1, 2, 4-10, and 13-16 relate to a composition comprising an HIV envelope antigen optimized for

immunogenicity, a second HIV antigen optimized for immunogenicity limited in claim 10 to be the *gag* gene product and combined with adjuvant protein, LTK63

Vajdy *et al.* teach intranasal immunization of mice with HIV envelope protein and an LTK63 adjuvant. Vajdy *et al.* also teach intranasal immunization of mice with an HIV gag protein and LTK63. Vajdy *et al.* do not teach any particular amount of the HIV envelope protein nor does it teach or suggest a composition comprising LTR72. The MPEP in section 2144.06 states, in part:

> "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)..."

Thus the combination of the two HIV antigens, *env* and *gag* gene products, with LTK63 is *prima facie* obvious under Vajdy, *et al.*

In regard to the importance of the claimed amount of the HIV envelope protein (0.1-1000 μg), the MPEP 2144.05 discusses the obviousness of optimization of ranges and is quoted in part below:

> "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) ...
>
> "see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")...
>
> "A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of

> the optimum or workable ranges of said variable might be characterized as routine experimentation. In re: Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)..."

Thus, in absence of supporting data suggesting otherwise, a *prima facie* case of obviousness is established when prior art teaches a use of particular component, the concentration of which is a result-effective variable. In the present instance, the concentration of HIV envelope protein is a result effective variable, as taught by Keefer MC, *et al*, as well as many others. Keefer *et al.* summarize their findings, in part, as: "Administration of the 640-micrograms dose of this rgp160 vaccine candidate relative to the lower doses was associated with increased immunogenicity, including higher rates of homologous neutralizing antibody responses..." Thus a *prima facie* case of obviousness has been established with regard to the use of specific amounts of antigen being used in the vaccine and claims 1, 2, 4-10 and 13-16 are properly and finally rejected under 35 U.S.C. 103(a) as being unpatentable over Vajdy, *et al.* in view of Keefer MC, *et al.*

The Office considered applicants' arguments regarding these claims and because of the reasons given above, we do not find the arguments persuasive and stand by our previous rejection of these claims.

Rejection of Claims 1, 11, and 12 Under 35 U.S.C. § 103: Claims 1, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vajdy, *et al.* in view of Keefer as applied to claims 1, 2, 4-10 and 13-16 above, and further in view of Kumar and Narayan, Haynes, Kang *et al.*, Tobery and Siliciano, Cease and Berzofsky and Vogel. Vajdy, *et al.* in view of Keefer *et al.* do not teach the use of other HIV antigens in

the composition of their anti-HIV vaccine. Kumar and Narayan teach the use of live, attenuated retroviral vaccines as a model of HIV infection using the SHIV/macaque model system. In particular, they teach the use of gp120 at a concentration in the amount of 100 and 50 μg per inoculation; they further teach the deletion of either or both *nef* and *vpu* genes from a SIV/HIV hybrid virus (SHIV) and use of either of two resultant mutant viruses as components of vaccine. Thus, applicants' assertion of uniqueness due to a specific mass of antigen used for inoculation is rejected as well as uniqueness of combination of *env*-derived proteins and other components of HIV.

The motivation for combination of HIV proteins as vaccine is that envelope protein alone would be insufficient to elicit an effective and complete immune response as taught by many researchers in the field. The applicants claim that the invention could be comprised of any of several HIV antigens and, in fact, the papers cited above teach many such combinations: Haynes teaches uses of envelope and gag proteins; Kang *et al.* teach use of env-gag virus like particles; Tobery and Siliciano teach the use of envelope and gag proteins; Cease and Berzofsky teach the use of envelope and several other HIV proteins; Vogel teaches several combinations of envelope and other (S)HIV including chemically inactivated retroviruses containing all of the retroviral structural proteins). In addition, Vogel teaches the importance of achieving immunological activation of both the humoral and cell-mediated arms of the immune system by judiciously choosing adjuvant and inoculation route. In light of the papers cited above and those cited by the previous examiner, it would indeed be obvious to

one ordinarily skilled in the art of vaccinology to combine one or more HIV antigens with a mucosal adjuvant such as LTK63 to broaden the scope of the immune response.

The Office has considered applicants' arguments regarding rejection of claims 1, 11, and 12; we find them unpersuasive for the reasons given above and stand by our previous rejection of these claims on the grounds of obviousness.

Rejection of Claims 32-36 Under 35 U.S.C. § 103: Claims 32-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vajdy, *et al.* in view of Keefer as applied to claims 1, 2, 4-10 and 13-16 above, and further in view of Kumar and Narayan.

Claims 32-36 refer to a composition of HIV envelope protein and a detoxified E. coli heat-labile toxin; claim 32 limits the amount of HIV envelope antigen to a range of between 1-300 μg, claim 33 further limits claim 32 to about 100 μg, claim 34 is a repetition of claim 33 in a different form, claim 35 limits claim 5 by identifying the HIV envelope antigen as Ogp140 and in the amount of about 300 μg, and claim 36 identifies an amino acid substitution of Ogp140 relative to native *env* gene products.

Vajdy *et al* teach intranasal immunization of mice with HIV envelope protein (both gp120 and Ogp140) and an LTK63 adjuvant. Vajdy *et al.* do not teach any particular amount of the HIV envelope protein nor does it. Kumar and Narayan further teach the use of live, attenuated retroviral vaccines as a model of HIV infection using the SHIV/macaque model system. In particular, they teach the use of gp120 at a concentration in the amount of 100 and 50 μg per inoculation. Thus, applicants' assertion of uniqueness due to a specific mass of antigen used for inoculation is rejected as well as uniqueness of the use of Ogp140 as antigen.

It would have been obvious to one of ordinary skill in the art to modify the composition of Vajdy *et al.* and Kumar and Narayan in order to combine Ogp140 in the amount of about 300 μg with either heat-labile *E coli*-derived toxin. One would have been motivated to do so, given the suggestion Kumar and Narayan, that the resultant vaccine would be more broadly based. There would have been a reasonable expectation of success, given the knowledge that partially inactivated SHIV in macaques elicit broad immune response, as taught by Kumar and Narayan, and also given the knowledge that certain heat-labile *E coli*-derived toxins also broaden the immune response, as taught by Vajdy *et al.* Thus the invention as limited by claims 32-36 was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made and the application is finally rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart W. Snyder whose telephone number is (571) 272-9945. The examiner can normally be reached on Mondays through Fridays between the hours of 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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